

IN THE SPECIFICATION

Please replace the paragraph beginning on page 4, line 8, with the following replacement paragraph:

The results of experiences made by the Inventors, operating with truncated forms of the DEN-2 ectodomain indicate that the nine carboxy-terminal amino acids of the M ectodomain (M32-40) constitute an intrinsic apoptotic sequence. The discovery of M32-40 brings to light a role for the small membrane M protein in DEN virus pathogenicity. Detailed comparison indicated that M32-40 of the four serotypes of DEN where more than 75% identical. Searches on nucleotide and protein databases showed that the nine-residue sequence responsible for the cytotoxic effect of the M ectodomain displayed no obvious similarity with any known cellular protein. Viscerotropic YF virus causes damage to liver cells in humans and hepatocytic apop-tosis has been observed in infected livers. Two live attenuated vaccine strains, 17D and French neurotropic virus (FNV) are known to have the ability to cause viscero-tropic disease. Comparison of the genomes of the YF vaccine strains 17D and French neurotropic virus (FNV) with the parental and other wild-type YF viruses revealed a common difference at position M36: the isoleucine residue at this position in the wild-type YF virus (Asibi) was replaced by a phenylalanine (17D vaccine strain) during attenuation. The Inventors demonstrate for the first time that the [[L36F]] I36F substitution observed in YF vaccine strains abolishes the death-promoting activity of the YF M ectodomain. The [[L36F]] I36F substitution also results in a reduction of the cytotoxicity of the DEN-2 ectodomain. Thus residue M36 not only plays an essential role for the efficient induction of apoptosis by peptides M32-40 containing it, but also the residue M36 is critical for the attenuation of viscerotropic flaviviruses.